Highlights of the 13th Asilomar Conference on Mass Spectrometry

Reviewed by O. David Sparkman
4045 Eagle Ridge Drive
Antioch, CA 94509

The Asilomar Conference on Mass Spectrometry was begun in 1980 by Laszlo Tokes, Ron Hass, and Arine Falick with Mass Spectrometry/Mass Spectrometry as its topic. The conference is now part of the annual series sponsored by the ASMS. Held at the Asilomar Conference Center in Pacific Grove, CA, November 5–9, 1997, the 1997 topic was Mass Spectrometry and Drug Discovery. Steven A. Carr (SmithKline Beecham Pharmaceuticals, King of Prussia, PA) and Bradford W. Gibson (University of California, San Francisco, CA) were the Program Chairmen. Now held annually, the Conference has been held at Asilomar every year except for one in which it was held in Colorado. The Asilomar Conference Center is an ideal location for this type of directed-focus meeting. It is secreted between Monterey and Carmel on the shore of the Pacific ocean. With its shared accommodations, group meals, great facilities for after-meeting discussions, and secluded surroundings, participants can immerse themselves in the topic in order to gain a complete appreciation of the oral and poster presentations as well as the specific area of science.

As can be seen from the titles in the six oral sessions and the poster presentations (see below), the meeting was somewhat divided between the use of mass spectrometry for the characterization of biopolymers and combinatorial chemistry. Both of these areas have a need for high sample throughput. Biopolymer analyses are being addressed with the development of microchip technology for the introduction of relative contamination-free analytes. The need in combinatorial chemistry is not so much to analyze the proliferation of samples but to develop ways to evaluate and manage the large amounts of data being produced.

Walter Moos (CEO of Mitokor Corporation, formerly Applied Genetics, San Diego, CA) in a type of keynote presentation entitled "Biotech & Pharma at the Proverbial Crossroads" showed his roots as one of the first people to champion the use of computer-assisted drug design, combinatorial chemistry, and high-volume screening in modern pharmaceutical research and development in that, although not stated, Dr. Moos implied that if combinatorial chemists have their way, they will consume all the matter in the universe to build their libraries. This was in conjunction with his statements about the vast volume of compounds that must be synthesized in order to find one that will eventually reach the market as a successful pharmaceutical product. He also made another interesting observation about the human life span once a treatment/prevention for all diseases and aging had been found. He said that actuaries had shown that people would then only have an average life span of 140 years because they would be killed as a result of an accident.

Along the lines of sample volume requirements reported by Dr. Moos was the need for better and faster computer technology to maintain the volume of data produced by these massive combinatorial libraries in Joseph A. Loo's (Parke-Davis, Ann Arbor, MI) presentation entitled "Monitoring Protein/RNA/Drug Interactions by ESI-MS." In some respects, it appears that mass spectrometry has come full circle. In the early days of GC/MS, the limitation was in managing the large volume of data. In today's high sample throughput that uses microchips and rapid acquisition techniques, the limiting factor is once again computing power and software design.

There was some discussion regarding instrumentation developments in the oral sessions; however, the thrust of the meeting was more toward the results obtained with mass spectrometry rather than new instrumentation. One instrumental point of significance is the improved performance of electrospray ionization at low flow rates. Several presenters continued to promote the benefits of electrospray combined with the Paul ion trap. Increased sensitivity compared to that obtained on the same manufacturer's triple-quadrupole mass-to-charge ratio analyzer was just one of the many benefits reported along with structural information that could be obtained from various stages of MS^n. Improvements in instrumental techniques, such as delayed extraction for the time-of-flight mass spectrometer, were also reported.

This meeting was a good mixture of reports on advances in drug discovery through the use of mass spectrometry and the development and refinement of mass spectral techniques to benefit further drug discovery. Gain Dollinger, Chiron Corporation, Emeryville, CA, pointed out that for a long period in the history of the role of mass spectrometry in drug discovery, advancements in the instrumentation and methods were the driving force behind the developments in the applications; however, today the application needs drive the developments of the instrumentation and methods. Jack Henion supported this philosophy with his statement, "It is easy to find a needle in a haystack when you have a magnet" when making reference to the high degree of specificity obtainable by today's mass spectral techniques.

From the presentations, it is clear that as biotechnology continues to drive the pharmaceutical industry, mass spectrometry will play an ever-increasing role. The advancement in desorption ionization techniques and the increase in sensitivity and specificity have made techniques such as matrix-assisted laser desorption/

1044-0305/98/$19.00
PII S1044-0305(98)00014-2
(J Am Soc Mass Spectrom 1998, 9, 545)

ionization, electrospray, and atmospheric pressure chemical ionization benchtop tools for the biotechnologist. Presenters were equally divided between those who are only interested in what the mass spectral data can tell them to aid in the understanding of complex biological mechanisms and those who are more concerned with how mass spectrometry provides this information so that they can develop techniques and instrumentation to address the next set of challenges.

The following oral presentations were made:

James A. McCloskey, University of Utah, Salt Lake City, UT, "Characterization of Oligonucleotides"

Daniel P. Little, Sequenom, San Diego, CA, "Toward High Throughput Chip-Based DNA Diagnostics by Maldi-MS"

Matthias Mann, European Molecular Biology Laboratories, Heidelberg, Germany, "Gene Function via the Analysis of Multi-Protein Complexes"

Jeffrey Shabanowitz, University of Virginia, Charlottesville, VA, "Sequencing Biologically Relevant Peptides at the Sub-Femtomole Level From Complex Mixtures"

Catherine Costello, Boston University Medical Center, Boston, MA, "MS Approaches to Glycan Analysis: Coping with Heterogeneity"

Bradford W. Gibson, University of California, San Francisco, CA, "Structure, Function and Therapeutic Design: Targeting Carbohydrates in Infectious Diseases"

David J. Harvey, Oxford University, Oxford, UK, "Characterization of Protein Bound Carbohydrates by MALDI-MS"

Anne-Marie Strang, Genetics Institute, Andover, MA, "Characterizing Protein Glycosylation: A General Strategy Combining and Enhancing HPAEC-PED and MS"

Mark Hemling, SmithKline Beecham Pharmaceuticals, King of Prussia, PA, "Analyzing the Tidal Wave of the Future"

Daniel Kassel, CombiChem, San Diego, CA, "Maximizing the Performance and Throughput of an Automated LC/MS System for the Characterization and Purification of Combinatorial Libraries"

Stephen Naylor, Mayo Clinic, Rochester, MN, "Mechanistic Studies of Noncovalent Complex Formation by ESI-MS-Role in Preclinical Investigations"

John Gilbert, Merck Research Laboratories, West Point, PA, "Use of LC-MS/MS for Drug Metabolism Studies in Support of Drug Discovery"

Walter Moos, CEO, Mitokor Corporation, San Diego, CA, "Biotech & Pharma at the Proverbial Crossroads"

James Vath, Millennium Pharmaceuticals, Inc., Cambridge, MA, "The Role of Mass Spectrometry in Genomic-Based Drug Discovery"

Reudi Aebersold, University of Washington, Seattle, WA, "MS-Based Techniques for the Analysis of Biological Systems"

Steven A. Carr, SmithKline Beecham Pharmaceuticals, King of Prussia, PA, "Characterizing Post-translational Modifications in Support of Protein Discovery"

Jack D. Henion, Cornell University, Ithaca, NY, "Revised LC/MS/MS Strategies for Meeting the Demands of Modern Drug Discovery Timelines"

Barry L. Karger, Northeastern University, Boston, MA, "New Directions in CE/MS and Microchip/MS"

Gavin Dollinger, Chiron Corporation, Emeryville, CA, "AS/MS @ ACMS-ASMS: A Practical Guide to Affinity Selection Mass Spectrometry as Applied to Drug Discovery"

Robert J. Anderegg, Glaxo-Wellcome, Research Triangle Park, NC, "Taking Another (and Another, and Another) Look at Bioaffinity Selection/Mass Spectrometry"

Brian Chait, Rockefeller University, New York, NY, "Rapid Approaches to Protein Identification and Characterization"

Jasna Peter-Katalinic, University of Muenster, Muenster, Germany, "Mass Spectrometry of Carbohydrate-Protein Interactions"

Joseph A. Loo, Parke-Davis, Ann Arbor, MI, "Monitoring Protein/RNA/Drug Interactions by ESI-MS"

The following posters were presented:

Julian P. Whitelegge, University of California, Los Angeles, CA, "Electrospray-Ionization Mass Spectrometry of Intact Intrinsic Membrane Receptors"

Margaret M. Sheil, University of Wollongong, Wollongong, Australia, "Rapid Determination of the Sequence Selectivity of DNA Alkylating Agents"

David Tolson, SmithKline Beecham Pharmaceuticals, Harlow, UK, "MALDI-TOF Sequencing of RNA Using Enzymatic and Chemical Methods"

Michael L. Gross, Ragulan Ramanthan, W. Zielinski, and T. P. Layoff, Washington University, St. Louis, MO, "Consistency Measures for (Poly)Peptide Pharmaceuticals: Electrospray Ionization Mass Spectrometry of Insulins with Deuterium Isotope Exchange"

John T. Stults and David Arnott, Genetech Inc., South San Francisco, CA, "Protein Differential Display and Mass Spectrometry Strategies for the Identification of Disease-Related Proteins"

Murray Hackett, University of Washington, Seattle, WA, "Determination of Lipid A Modifications by MALDI-TOF, Tandem Quadrupole and Ion Trap Mass Spectrometry"

Katalin Medzihradszky, University of California, San Francisco, CA, "Studies on N-Glycosylation of Recombinant Factor VIII"

Jason Rouse and Anne-Marie Strang, Genetics Institute, Andover, MA, "Structural Characterization of Endole-Released N-Linked Oligosaccharides by High PH Anion-Exchange Chromatography Matrix-Assisted Laser Desorption/Ionization Post-Source Decay Time-of-Flight Mass Spectrometry, and Glycosides Digestion"

D. S. Wagner, H. M. Geyser, C. J. Markworth, and F. J. Schoeney, Glaxo-Wellcome, Inc., Diversity Sciences

Department, Research Triangle Park, NC, "Mass Encoding of Combinatorial Libraries"

B. Moldover, J. Cavalcoli, R. Van Bogelen, T. Stevenson, and J. Loo, Parke-Davis Pharmaceutical Research Molecular Biology Department, and K. Ogorzalek, R. Leo, C. Mitchell, and P. Andrew, Department of Chemistry University of Michigan, "A New Technology for High Throughput Proteome Mapping From 2-D Gels"

K. B. Lim, Lin Guo, J. S. Gunn, M. M. Daniels, R. P. Darveau, M. Hackett, and Samuel Miller, University of Washington, "Lipid A Modification by Salmonella Typhimurium and Pseudomonas Aeruginosa"